A Liquid Path to Lung Disease

Early Arsenic Exposure and Effects in Young Adults

Increased rates of cancer and mortality have been documented in areas of the world where drinking water contains high concentrations of naturally occurring arsenic. A new study by a group of Californian and Chilean researchers now provides strong evidence of a link in humans between prenatal and early childhood arsenic exposure and significantly higher rates of lung disease in young adulthood [***EHP* 114:1293–1296; Smith et al.**].

A big gulp of news. The link between early arsenic exposure and later lung disease is the first such association to be confirmed in humans.

Both malignant and nonmalignant lung disease are known to develop with exposure to arsenic in drinking water. Recent evidence from a project in India by the same research group showed decreased lung function similar to that of smokers in adults exposed to the semimetallic carcinogen.

The current study took advantage of a unique opportunity to study the long-term health effects of a discrete prenatal and early childhood exposure. From 1958 to 1970, the water supply for the neighboring Chilean cities of Antofagasta and Mejillones was supplemented with water from rivers with arsenic concentrations near 1,000 µg/L, 100 times the current acceptable standard for arsenic concentration in the United States. With the 1971 activation of an arsenic removal plant, however, levels plummeted to about 90 µg/L and have continued to drop ever since.

The research team studied mortality data obtained from Chile's Ministry of Health for the years 1989 through 2000 for all 13 regions of the country. They divided the population into two groups: individuals born between 1958 and 1970 (who likely would have had prenatal arsenic exposure if their mothers lived in Antofagasta or Mejillones) and those born between 1950 and 1957 (who likely would have had childhood but not prenatal exposure if they lived in either of the two cities). The researchers also divided overall deaths for Chile into two groups: residents of Antofagasta and Mejillones, and residents of all other regions. They used the *International Classification of Diseases, Ninth Revision,* to code causes of death, including lung cancer and bronchiectasis, a form of chronic respiratory disease.

The investigators' findings show a distinct connection between prenatal and early childhood exposure to arsenic and lung disease–related mortality before age 50. Lung cancer death rates for those exposed to arsenic in early childhood were 7 times higher than those for the rest of the Chilean population, and bronchiectasis death rates were 12 times higher. In cases where exposure occurred both prenatally and in early childhood, lung cancer death rates were 6 times higher and bronchiectasis death rates were 46 times higher than those for the rest of the population.

The authors believe these results describe the highest increase in death rates for arsenic-related lung cancer and bronchiectasis ever documented among young adults, and add that this study is one of the first to provide evidence of human adult disease resulting from prenatal and early childhood exposure to any environmental toxicant. They conclude that an increase in young adult mortality should be of concern to public health officials, and should influence future decisions regarding sources of drinking water. **–Tanya Tillett**

Ultrafines' Quick Neurological Hit

Particles Take a Direct Route to the Brain

Proof of the penetrating capabilities of tiny particles continues to emerge. A team of U.S. researchers has just added to and clarified the existing evidence by documenting significant, rapid accumulations of inhaled ultrafine manganese oxide particles in the lung and many brain regions [***EHP* 114:1172–1178; Elder et al.**]. They also demonstrated that particles don't need to dissolve to spread, and that inhalation pathways can be more efficient than circulatory ones.

The researchers evaluated the translocation and tissue distribution of manganese oxide ultrafines in rats that had inhaled a nearly insoluble form of these solid particles for six hours per day, at a concentration in the mid-range typically experienced by welders. After 12 days of exposure, the manganese concentration in the olfactory bulb (a region of the brain that abuts the nasal cavity) had increased about 3.5-fold. At the same time, lung manganese concentrations doubled, and there were small but significant increases in other brain regions, such as the cerebellum, the frontal cortex, and the striatum.

The inhaled ultrafines didn't cause obvious lung inflammation. However, in the brain several markers of inflammation and stress response, including tumor necrosis factor and macrophage inflammatory protein, increased by anywhere from about 2- to 30-fold.

To determine how inhaled manganese oxide ultrafines spread, the team closed the right nostril of several of the rats and had them inhale manganese oxide solely through the left nostril. They found that the vast majority of manganese quickly accumulated in the left olfactory bulb. This suggested that very little of the accumulation was due to other routes, such as dissolution and distribution via the circulatory system; otherwise, the manganese would have appeared in both olfactory bulbs.

The negligible role of the circulatory system contrasted with the findings of another manganese study, but that study utilized poorly soluble manganese phosphate particles that were several orders of magnitude larger than the approximately 30-nm manganese oxide agglomerates used here. The particles in the current study were about one-sixth the diameter of the olfactory neurons, along which the agglomerates moved into the brain.

These findings, as well as those of other studies of tiny particles such as carbon, gold, poliovirus, and engineered nanoparticles, suggest to the researchers that much more research is needed to determine if other inhaled ultrafines can also rapidly disseminate and cause effects throughout animal bodies. **–Bob Weinhold**

Hearing Loss, Loud and Clear

Combined Effect of Noise and Toluene in Workers

Animal studies have clearly shown that simultaneous exposure to noise and toluene, a clear organic solvent widely used in various manufacturing industries, causes hearing loss. Studies of this interaction in the workplace have been limited, however, and their results inconclusive. Research now establishes, for the first time, a strong correlation between hearing loss in workers and their simultaneous exposure to noise and toluene [***EHP* 114:1283–1286; Chang et al.**].

Conducted in a Taiwan adhesive factory, the study included three male study groups: 58 workers exposed only to noise (an average of 85 A-weighted decibels), 58 workers exposed to both toluene and noise, and 58 administrative workers. Air samples were collected from the working areas of the three groups, and sound pressure level meters were used to assess noise levels in the same areas. The researchers also calculated the time-weighted average of noise levels for each group.

The researchers collected data through interviews and physical examinations of the participants, including information on lifestyle and sociodemographic variables such as age, whether respondents smoked or drank, and use of hearing protection. They also administered hearing tests in a soundproof room. A physician conducted an otopharyngeal exam to screen for otitis and other ear problems.

Stereophonic impact? New human data confirm the interactive effect of toluene and noise.

Toluene exposure appeared to increase the risk of hearing loss by as much as six times when compared to loss related to noise exposure only. The workers with the lowest toluene exposure had only a slightly lower risk of hearing loss when compared with those with higher levels of toluene exposure.

The authors acknowledge that the study had three limitations: the small sample size, the inability to measure exposure to high levels of toluene over a long work history, and the lack of available data for estimating hearing loss caused by exposure to toluene alone. They conclude, however, that their study does prove that workers face a greater risk of hearing loss when simultaneously exposed to toluene and noise compared to exposure to noise alone.

The authors believe the current established workplace standard for toluene of 100 ppm does not, by itself, protect against hearing loss for those workers exposed simultaneously to noise. They suggest that effective intervention is needed to improve the occupational safety of such individuals. **–Ron Chepesiuk**

PAHs and Cognitive Impairment

Prenatal Exposure Catches Up with Toddlers

Previous studies have documented reduced fetal growth and developmental impairment resulting from exposure to environmental toxicants such as tobacco smoke. Now researchers at the Columbia Center for Children's Environmental Health implicate another prenatal exposure in causing health effects, demonstrating for the first time that exposure to airborne polycyclic aromatic hydrocarbons (PAHs) *in utero* may affect cognitive development during childhood [***EHP* 114:1287–1292; Perera et al.**].

PAHs are introduced into the environment by combustion—car, truck, or bus exhaust, power generation, and cigarette smoking are just a few sources—and are transferred across the placenta. Urban populations have greater exposure to PAHs and therefore may be especially at risk for subsequent adverse health and developmental effects.

As part of the broader multiyear Mothers and Children Study, the researchers studied a cohort of 183 children of nonsmoking women living in the Washington Heights, Central Harlem, and South Bronx neighborhoods of New York City. They obtained demographic, residential, health, and environmental exposure information by administering a questionnaire during the mothers' last trimester of pregnancy. They also monitored the mothers' personal air exposures during the third trimester using backpack monitors.

Umbilical cord blood was collected and analyzed for cotinine, heavy metal, and pesticide content. Lead concentration was analyzed in a subset of 135 subjects. During postnatal follow-up interviews, the research team recorded any changes in residence, tobacco smoke exposure, or other conditions. The children's cognitive and psychomotor development was assessed at 1, 2, and 3 years of age using the Bayley Scales of Infant Development–Revised; the mothers also answered questionnaires on their children's behavior.

Although they noted no significant effect on behavior or cognitive or psychomotor development at ages 1 or 2, the Columbia investigators found that the 3-year-olds who had higher prenatal exposure to PAHs scored on average 5.69 points lower on cognitive tests than the less-exposed children, even when controlling for other exposures and socioeconomic factors. The higher-exposed children also had twice the odds of developmental delay, suggesting an increased risk for performance deficits in language, reading, and math in the first years of school.

Thought leader. Prenatal exposure to PAHs may affect cognitive development later on.

The authors acknowledge some limitations of the study, including small sample size, lack of air monitoring data for all three trimesters, and lack of postnatal data for personal air PAH concentrations and lead exposure. They conclude that additional studies should be conducted to confirm their results, especially since limited performance in the early school years can provide an indication of future suboptimal school performance. **–Tanya Tillett**

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